

09/392,682

---

Printed by EAST

---

**UserID:** JLee6 *original examiner ; restricted claims*

**Computer:** WS10958

**Date:** 05/10/2000

**Time:** 20:01

	Type	L #	Hits	Search Text	DBs	Time Stamp	C o m m e n t s	E r r o r s
1	BRS	L1	3814	gene adj therapy	USPAT	2000/05/10 19:59		0
2	BRS	L2	2	small near fragment near homologous near replacement	USPAT	2000/05/10 19:59		0

(FILE 'HOME' ENTERED AT 20:08:15 ON 10 MAY 2000)

FILE 'MEDLINE' ENTERED AT 20:08:20 ON 10 MAY 2000

L1	0 S	HOMOLOGOUS DNA REPLACEMENT
L2	18 S	HOMOLOGOUS REPLACEMENT
L3	11505 S	GENE? THERAP?
L4	321 S	L3 AND REPLACEMENT
L5	10 S	L4 AND HOMOLOGOUS
L6	49572 S	(CF OR CYSTIC FIBROSIS)
L7	13 S	L6 AND L4
L8	13 S	L7 AND L3

L8 ANSWER 3 OF 13 MEDLINE  
 AN 1998015741 MEDLINE  
 DN 98015741  
 TI Review article: **gene therapy** in gastroenterology and  
 hepatology.  
 AU Forbes S J; Hodgson H J  
 CS Liver Group Laboratory, Royal Postgraduate Medical School, London, UK.  
 SO ALIMENTARY PHARMACOLOGY AND THERAPEUTICS, (1997 Oct) 11 (5) 823-36. Ref:  
 98  
 Journal code: A5D. ISSN: 0269-2813.  
 CY ENGLAND: United Kingdom  
 DT Journal; Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)  
 (REVIEW, TUTORIAL)  
 LA English  
 FS Priority Journals  
 EM 199802  
 AB **Gene therapy** for diseases of the gastrointestinal  
 tract is an exciting prospect because of the fundamental cure that is  
 potentially available. The gastrointestinal system, and especially the  
 liver, is an area that will be central to the development of **gene**  
**therapy**. Techniques for gene **replacement** include  
 homologous recombination and gene augmentation. For the treatment of  
 cancer antisense strategy, pro-drug activation systems and gene  
 immunotherapy are being investigated. Gene-carrying vectors divide into  
 viral- and non-viral-based vectors, each with advantages and limitations.  
 The accurate delivery of these vectors to sufficient numbers of target  
 cells in vivo is still a major barrier to clinical use. Diseases that may  
 be helped by **gene therapy** include: gastrointestinal  
 malignancies, viral hepatitis, the haemophilias, hypercholesterolaemia,  
 alpha 1-antitrypsin deficiency, and metabolic diseases of the liver and  
**cystic fibrosis**. In this review we will outline the  
 principles of **gene therapy**, delivery vectors under  
 investigation, diseases that may benefit from this technology and some of  
 the remaining problems to be overcome.  
 CT Check Tags: Human; Support, Non-U.S. Gov't  
 \*Gastrointestinal Diseases: TH, therapy  
 Gastrointestinal Neoplasms: TH, therapy  
 \***Gene Therapy**  
 Hemophilia A: TH, therapy  
 Hepatitis, Viral, Human: TH, therapy  
 \*Liver Diseases: TH, therapy

8 ANSWER 4 OF 13 MEDLINE  
AN 97420210 MEDLINE  
DN 97420210  
TI CFTR gene transduction in neonatal rabbits using an adeno-associated virus (AAV) vector.  
AU Rubenstein R C; McVeigh U; Flotte T R; Guggino W B; Zeitlin P L  
CS Eudowood Division of Pediatric Respiratory Sciences, Johns Hopkins Medical Institutions, Baltimore, MD, USA.  
NC P01HL51811 (NHLBI)  
SO GENE THERAPY, (1997 May) 4 (5) 384-92.  
Journal code: CCE. ISSN: 0969-7128.  
CY ENGLAND: United Kingdom  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 199711  
EW 19971104  
AB Patients with **cystic fibrosis** develop lung disease after birth, therefore CFTR gene **replacement** therapy should be most efficacious in the neonatal period prior to the onset of pulmonary damage. An adeno-associated virus (AAV) vector, SA306 (Flotte TR et al Proc Natl Acad Sci USA 1993; 90: 10613-10617), which contains the AAV inverted terminal repeats flanking the human CFTR cDNA linked to an amino-terminal epitope tag, was used to transduce a human CFTR fusion protein into neonatal New Zealand white rabbits. Vector inocula of  $1 \times 10^5$  to  $5 \times 10^{10}$  particles were given by intratracheal instillation on day 3 of life and the rabbit lungs were studied at 3 or 4 days, 2-6 weeks, or 6 months after infection; the 2-6 week time-point corresponds to the completion of the alveolar phase of lagomorph lung development. Vector DNA was detected by an in situ polymerase chain reaction (PCR) using vector-specific primers at up to 6 weeks after inoculation. Human CFTR mRNA was detected by Northern analysis at up to 2 weeks after vector inoculation, and by a reverse transcriptase PCR assay at up to 3 weeks after infection. Epithelial expression of the human CFTR fusion protein was detected using antisera to both the human CFTR R domain and the amino-terminal epitope at up to 6 weeks after vector inoculation. Vector DNA, mRNA, or human CFTR immunoreactivity were not observed at the 6 month time-point. Rabbits infected with SA306 were clinically indistinguishable from their uninfected litter mates. These data indicate that CFTR gene transduction using an AAV vector is feasible in the neonatal rabbit, and that expression of vector-derived CFTR persists throughout the alveolar phase of lung development. The apparent lack of vector persistence after the alveolar phase may reflect dilution of transduced cells by further lung growth or a lack of transduction of pulmonary epithelial stem cells.

CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.  
Adenoviridae  
Animals, Newborn  
\***Cystic Fibrosis Transmembrane Conductance Regulator: GE, genetics**  
Gene Expression  
\***Gene Therapy: MT, methods**  
Genetic Vectors  
Immunohistochemistry  
Lung: CH, chemistry  
Polymerase Chain Reaction  
Rabbits

\*Transfection  
 RN 126880-72-6 (Cystic Fibrosis Transmembrane Conductance Regulator)  
 CN 0 (Genetic Vectors)

L8 ANSWER 5 OF 13 MEDLINE  
 AN 97358591 MEDLINE  
 DN 97358591  
 TI Incomplete rescue of **cystic fibrosis** transmembrane  
 conductance regulator deficient mice by the human CFTR cDNA.  
 AU Rozmahel R; Gyomai K; Plyte S; Nguyen V; Wilschanski M; Durie P; Bear C  
 E; Tsui L C  
 CS Department of Genetics, The Hospital for Sick Children, Toronto, Ontario,  
 Canada.  
 SO HUMAN MOLECULAR GENETICS, (1997 Jul) 6 (7) 1153-62.  
 Journal code: BRC. ISSN: 0964-6906.  
 CY ENGLAND: United Kingdom  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 199710  
 EW 19971005  
 AB We have used a mouse model to study the ability of human CFTR to correct  
 the defect in mice deficient of the endogenous protein. In this model,  
 expression of the endogenous Cftr gene was disrupted and replaced with a  
 human CFTR cDNA by a gene targeted 'knock-in' event. Animals homozygous  
 for the gene **replacement** failed to show neither improved  
 intestinal pathology nor survival when compared to mice completely  
 lacking  
 CFTR. RNA analyses showed that the human CFTR sequence was transcribed  
 from the targeted allele in the respiratory and intestinal epithelial  
 cells. Furthermore, in vivo potential difference measurements showed that  
 basal CFTR chloride channel activity was present in the apical membranes  
 of both nasal and rectal epithelial cells in all homozygous knock-in  
 animals examined. Ussing chamber studies showed, however, that the  
 cAMP-mediated chloride channel function was impaired in the intestinal  
 tract among the majority of homozygous knock-in animals. Hence, failure  
 to  
 correct the intestinal pathology associated with loss of endogenous CFTR  
 was related to inefficient functional expression of the human protein in  
 mice. These results emphasize the need to understand the tissue-specific  
 expression and regulation of CFTR function when animal models are used in  
**gene therapy** studies.  
 CT Check Tags: Animal; Human; Support, Non-U.S. Gov't  
 Alleles  
 \*Cystic Fibrosis: GE, genetics  
 \*Cystic Fibrosis Transmembrane Conductance Regulator: DF,  
 deficiency  
 \*Cystic Fibrosis Transmembrane Conductance Regulator: GE, genetics  
 Cystic Fibrosis Transmembrane Conductance Regulator: ME,  
 metabolism  
 Electrophysiology  
 Forskolin: PD, pharmacology  
 Homozygote  
 Intestines: DE, drug effects  
 Intestines: PH, physiology  
 Mice  
 \*Mice, Transgenic: GE, genetics  
 Phenotype  
 Recombinant Proteins: GE, genetics  
 Recombinant Proteins: ME, metabolism  
 Recombination, Genetic  
 Transgenes

RN 126880-72-6 (Cystic Fibrosis Transmembrane Conductance Regulator)  
 ; 66428-89-5 (Forskolin)  
 CN 0 (Recombinant Proteins)

L8 ANSWER 10 OF 13 MEDLINE  
 AN 96066888 MEDLINE  
 DN 96066888  
 TI Recent advances in the application of **gene therapy** to human disease.  
 AU Hanania E G; Kavanagh J; Hortobagyi G; Giles R E; Champlin R; Deisseroth A  
 B  
 CS Department of Hematology, University of Texas M.D. Anderson Cancer Center, Houston, USA.  
 NC P01 CA49639 (NCI)  
 P01 CA55164 (NCI)  
 SO AMERICAN JOURNAL OF MEDICINE, (1995 Nov) 99 (5) 537-52. Ref: 73  
 Journal code: 3JU. ISSN: 0002-9343.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)  
 (REVIEW, TUTORIAL)  
 LA English  
 FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals  
 EM 199602  
 AB PURPOSE: To review the recent advances in the application of genetic modification strategies to the therapy of human diseases for which a molecular defect is known. METHODS: A computerized data bank search, the minutes of the National Institutes of Health (NIH) Recombinant DNA Advisory Committee published in the Federal Record, and reports of human clinical trials were used as data sources for this review. Clinical trials included in this review were published in the literature or approved by the NIH Recombinant DNA Advisory Committee. STUDY SELECTION: Evaluations of the efficacy of genetic modification strategies in clinical trials in human and in animal models are summarized. The design and outcome of the genetic modification strategies employed are reviewed for 16 marking trials, 16 gene **replacement** trials for molecular deficiency diseases, 3 chemoprotection and 4 chemotherapy sensitization trials, 11 cancer vaccine trials, 2 antisense oligonucleotide trials, and 3 molecular immunotherapy trials. DATA SYNTHESIS: The marking trials have shown that residual leukemia cells in the infused autologous marrow can contribute to relapse following autologous bone marrow transplants. The use of genetic modification for the **replacement** of missing or deficient genes in severe combined immunodeficiency, familial hypercholesterolemia, and **cystic fibrosis** has been associated with encouraging results so far. Clinical **genetic therapy** trials involving cancer vaccines, antisense oligonucleotides, adoptive immunotherapy with genetically modified T cells, delivery vectors containing interleukin-1 receptor inhibitor for arthritis, **replacement** strategies for storage diseases, and genetic suppression of human immunodeficiency viral replication are just commencing. CONCLUSIONS: The clinical application of genetic modification techniques has thus far been successful in the beginning phases of this field. These early results suggest that continuation of **gene therapy** trials designed to correct the molecular changes that lead to disease states in humans is warranted. Evaluation of such clinical trials in the future may be based on the analysis of assays for short-term surrogate endpoints, as well as on the therapeutic outcomes of the trial, such as survival or remission.

• CT. Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.  
Bone Marrow Transplantation  
Clinical Trials

**\*Gene Therapy**

Gene Therapy: MT, methods

HIV Infections: TH, therapy

Immunotherapy

Neoplasms: TH, therapy



L8 ANSWER 12 OF 13 MEDLINE  
 AN 94167392 MEDLINE  
 DN 94167392  
 TI The new frontier: gene and oligonucleotide therapy.  
 AU Schreier H  
 CS Center for Lung Research, Vanderbilt University School of Medicine,  
 Nashville, TN 37232-2650..  
 SO PHARMACEUTICA ACTA HELVETIAE, (1994 Jan) 68 (3) 145-59. Ref: 105  
 Journal code: POE. ISSN: 0031-6865.  
 CY Switzerland  
 DT Journal; Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)  
 (REVIEW, TUTORIAL)  
 LA English  
 EM 199406  
 AB Gene and oligonucleotide therapy are emerging as clinically viable  
 therapeutic regimens for genetic, neoplastic, and infectious diseases.  
 Approaches include insertion of human genes in viral vectors including  
 recombinant retrovirus, adenovirus, adeno-associated virus, and herpes  
 simplex virus-1, or recombinant bacterial plasmids. Viral vectors  
 transfect cells directly; plasmid DNA is delivered with the help of  
 cationic liposomes (lipofection), polylysine conjugates, gramicidin S,  
 artificial viral envelopes or other such intracellular carriers. Major  
 areas of interest include **replacement** of the **cystic**  
**fibrosis** transmembrane regulator gene and the alpha 1-antitrypsin  
 gene; arrest of human immunodeficiency virus infection; and reversal of  
 tumorigenicity and cancer immunization, among others. Oligonucleotide  
 therapy is principally focusing on the same areas, although the approach  
 is to halt DNA transcription or messenger RNA translation with  
 code-blocking triple-helix-forming or "antisense" oligomers.  
 Contributions  
 from the pharmaceutical sciences are expected in pharmaceutical  
 chemistry,  
 drug delivery systems design, analytical chemistry, and biopharmaceutics.  
 CT Check Tags: Animal; Human; Support, Non-U.S. Gov't  
 \*Gene Therapy  
 \*Oligonucleotides  
 CN 0 (Oli

L8 ANSWER 13 OF 13 MEDLINE  
 AN 93282540 MEDLINE  
 DN 93282540  
 TI Molecular biology and therapy of disease.  
 AU Samara G; Sawicki M P; Hurwitz M; Passaro E Jr  
 CS Department of Surgery, UCLA School of Medicine, Wadsworth Veterans  
 Administration Medical Center 90073..  
 SO AMERICAN JOURNAL OF SURGERY, (1993 Jun) 165 (6) 720-7. Ref: 7  
 Journal code: 3Z4. ISSN: 0002-9610.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)  
 (REVIEW, TUTORIAL)  
 LA English  
 FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals  
 EM 199309  
 AB Molecular biology will have a profound impact upon the treatment of  
 disease. Molecular techniques provide protein products for treatment of  
 more diseases each year. The understanding of pathophysiology at the  
 molecular level allows for improved drug design. Antisense technology can  
 selectively control gene expression. **Gene therapy** is  
 potentially the most important aspect of molecular biology. Physical and  
 viral transduction mechanisms are being developed toward this end. Gene  
**replacement**, creation of antisense oligonucleotides, and prodrug  
 strategies are being developed. Currently, gene **replacement** and  
 prodrug therapy are feasible in at least a few cases, but further study  
 will yield additional applications.  
 CT Check Tags: Human  
 Antisense Elements (Genetics)  
 Child  
**Cystic Fibrosis: CO, complications**  
**\*Gene Therapy**  
 Neoplasms: TH, therapy  
 Pancreatitis: ET, etiology  
 Pancreatitis: TH, therapy  
 Prodrugs: TU, therapeutic use  
 Respiratory Tract Infections: ET, etiology  
 Respiratory Tract Infections: TH, therapy  
 Transfection  
 CN. 0 (Antisense Elements (Genetics)); 0 (Prodrugs)

FILE 'MEDLINE' ENTERED AT 19:52:47 ON 10 MAY 2000

L1 11505 S GENE? THERAP?  
L2 3 S L1 AND (SMALL FRAGMENT HOMOLOGOUS REPLACEMENT)  
L3 3 S L1 AND (HOMOLOGOUS REPLACEMENT)  
L4 18 S HOMOLOGOUS RE

L2 ANSWER 1 OF 3 MEDLINE  
 AN 2000024476 MEDLINE  
 DN 20024476  
 TI Site-directed alteration of genomic DNA by **small-fragment homologous replacement**.  
 AU Goncz K K; Gruenert D C  
 CS Cardiovascular Research Institute, University of California, San Francisco, USA.  
 SO METHODS IN MOLECULAR BIOLOGY, (2000) 133 85-99.  
 Journal code: BU3. ISSN: 1064-3745.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 200002  
 EW 20000204  
 CT Check Tags: Human  
 Blotting, Southern  
 Cell Line  
 Cystic Fibrosis Transmembrane Conductance Regulator: GE, genetics  
 DNA: AN, analysis  
 \*Gene Targeting: MT, methods  
**Gene Therapy**  
 Genome, Human  
 Liposomes: CH, chemistry  
 Mutagenesis, Site-Directed  
 Oligodeoxyribonucleotides  
 \*Recombination, Genetic  
 Reverse Transcriptase Polymerase Chain Reaction  
 RNA: AN, analysis  
 Transfection  
 RN 126880-72-6 (Cystic Fibrosis Transmembrane Conductance Regulator);  
 63231-63-0 (RNA); 9007-49-2 (DNA)  
 CN 0 (Oligodeoxyribonucleotides)

L2 ANSWER 2 OF 3 MEDLINE  
 AN 1999030259 MEDLINE  
 DN 99030259  
 TI Targeted replacement of normal and mutant CFTR sequences in human airway epithelial cells using DNA fragments.  
 AU Goncz K K; Kunzelmann K; Xu Z; Gruenert D C  
 CS Cardiovascular Research Institute, Gene Therapy Core Center and Cystic Fibrosis Research Center and Department of Laboratory Medicine and Stomatology, University of California, San Francisco, CA 94143, USA.  
 NC DK46002 (NIDDK)  
 DK47766 (NIDDK)  
 SO HUMAN MOLECULAR GENETICS, (1998 Nov) 7 (12) 1913-9.  
 Journal code: BRC. ISSN: 0964-6906.  
 CY ENGLAND: United Kingdom  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 199902  
 EW 19990204  
 AB Recent studies have reported that mutant genomic cystic fibrosis (CF) transmembrane conductance regulator ( CFTR ) sequences can be corrected  
 in  
 transformed CF airway epithelial cell lines by targeted replacement with small fragments of DNA with wild-type sequence. To determine if the observed genotype modification following **small fragment**

homologous replacement (SFHR) was limited to transformed CF cell lines, further studies were carried out in both transformed and non-transformed primary normal airway epithelial cells. The endogenous genotype of these normal cell lines was modified following liposome or dendrimer transfection using DNA fragments with DeltaF508 CFTR sequence (488 nt, complementary single strands) designed to also contain a unique restriction enzyme cleavage site (Xho I). Replacement at the appropriate genomic locus by exogenous DeltaF508 CFTR DNA and its expression as mRNA was demonstrated by PCR amplification of genomic DNA and mRNA-derived cDNA as well as Xho I digestion of the PCR products. These studies show that SFHR occurs in both transformed and non-transformed primary human airway epithelial cells and indicate that single base substitution (the silent mutation giving rise to the Xho I site) and deletion or insertion of at least three consecutive bases can be achieved in both normal and CF epithelial cells. Furthermore, these studies reiterate the potential of SFHR as a strategy for a number of gene targeting applications, such as site-specific mutagenesis, development of transgenic animals, development of isogenic cell lines and for **gene therapy**.

CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.  
 Binding Sites: GE, genetics  
 Cell Line, Transformed  
 Cells, Cultured  
 Cystic Fibrosis: GE, genetics  
 Cystic Fibrosis: PA, pathology  
 \*Cystic Fibrosis Transmembrane Conductance Regulator: GE, genetics  
 Deoxyribonucleases, Type II Site-Specific: ME, metabolism  
 DNA: AN, analysis  
 \*DNA: GE, genetics  
 DNA: ME, metabolism  
 Epithelial Cells: CY, cytology  
 \*Epithelial Cells: ME, metabolism  
 Eukaryotic Cells: CY, cytology  
 Eukaryotic Cells: ME, metabolism  
 \*Gene Targeting  
 Mutation  
 Respiratory System: CY, cytology  
 Respiratory System: ME, metabolism  
 Reverse Transcriptase Polymerase Chain Reaction  
 RNA: AN, analysis

RN 126880-72-6 (Cystic Fibrosis Transmembrane Conductance Regulator);  
 63231-63-0 (RNA); 9007-49-2 (DNA)

CN EC 3.1.21.- (endodeoxyribonuclease XhoI); EC 3.1.21.4  
 (Deoxyribonucleases,  
 Type II Site-Specific)

L2 ANSWER 3 OF 3 MEDLINE  
 AN 97064949 MEDLINE  
 DN 97064949  
 TI Gene targeting of CFTR DNA in CF epithelial cells.  
 AU Kunzelmann K; Legendre J Y; Knoell D L; Escobar L C; Xu Z; Gruenert D C  
 CS Cardiovascular Research Institute, University of California, San  
 Francisco, California 94143, USA.  
 SO GENE THERAPY, (1996 Oct) 3 (10) 859-67.  
 Journal code: CCE. ISSN: 0969-7128.  
 CY ENGLAND: United Kingdom  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 199707  
 EW 19970703  
 AB A goal of cystic fibrosis (CF) **gene therapy** is correction of the mutant CF transmembrane conductance regulator (CFTR) gene with wild-type (wt) DNA sequences to restore normal CFTR protein and function. Experiments with wtCFTR cDNA expression vectors have shown that the Cl ion transport phenotype associated with CF can be corrected to

resemble that in normal cells. An alternative to cDNA-based **gene therapy** strategies is one that corrects endogenous mutant sequences by targeted replacement with the wt homologue. To test whether such a strategy was feasible, a **small fragment homologous replacement** (SFHR) strategy was used to replace specific genomic sequences in human epithelial cells. Small fragments of genomic wtCFTR DNA were transfected into transformed CF epithelial cells. Replacement by exogenous CFTR DNA at the appropriate genomic locus and its expression as mRNA was indicated by: (1) allele-specific polymerase chain reaction (PCR) amplification of genomic DNA and mRNA-derived cDNA; and (2) hybridization of PCR products with allele-specific probes. In addition, the functional activity of CFTR protein was determined by whole cell patch clamp. Southern hybridization and patch clamp analyses suggested that approximately 1 in 100 CF cells underwent a homologous replacement event that resulted in intact Cl transport.

CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.  
Cell Line

\*Cystic Fibrosis

Cystic Fibrosis: PA, pathology

\*Cystic Fibrosis Transmembrane Conductance Regulator: GE, genetics

DNA: AN, analysis

Epithelium: CY, cytology

\*Gene Targeting: MT, methods

Patch-Clamp Techniques

RNA: AN, analysis

RN 126880-72-6 (Cystic Fibrosis Transmembrane Conductance Regulator);  
63231-63-0 (RNA); 9007-49-2 (DNA)

L4 ANSWER 14 OF 18 MEDLINE  
AN 91043073 MEDLINE  
DN 91043073  
TI Gene replacement in parasitic protozoa [see comments].  
CM Comment in: Nature 1990 Nov 8;348(6297):109  
AU Cruz A; Beverley S M  
CS Department of Biological Chemistry and Molecular Pharmacology, Harvard  
Medical School, Boston, Massachusetts 02115.  
SO NATURE, (1990 Nov 8) 348 (6297) 171-3.  
Journal code: NSC. ISSN: 0028-0836.  
CY ENGLAND: United Kingdom  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals; Cancer Journals  
EM 199102

L4 ANSWER 13 OF 18 MEDLINE  
AN 92404749 MEDLINE  
DN 92404749  
TI Long regions of homologous DNA are incorporated into the tobacco plastid  
genome by transformation.  
AU Staub J M; Maliga P  
CS Waksman Institute, Rutgers, State University of New Jersey, Piscataway  
08855-0759..  
SO PLANT CELL, (1992 Jan) 4 (1) 39-45.  
Journal code: BJU. ISSN: 1040-4651.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 199212